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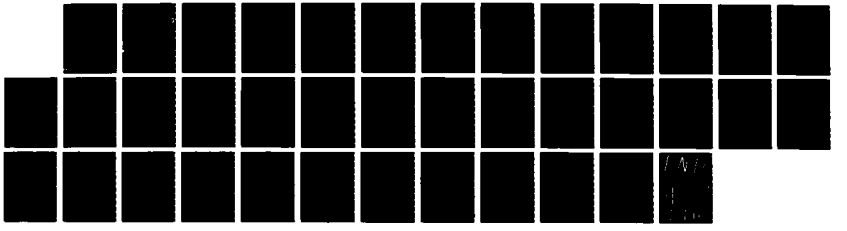

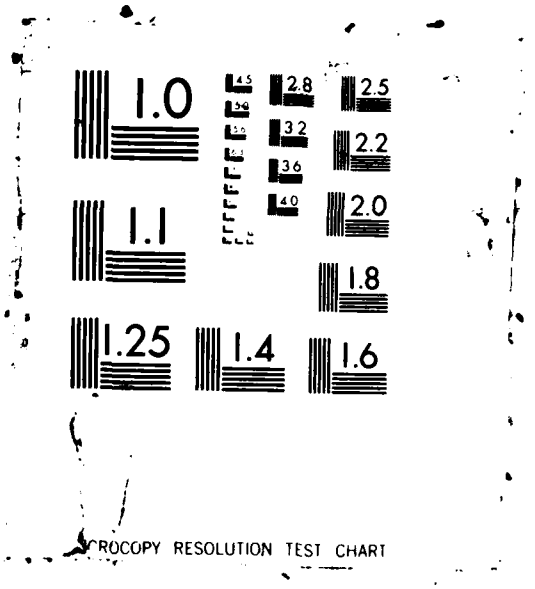
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original mean while associated values for $\dot{V}E$, f and T_V were not different, suggesting that responses which improve or maintain exercise performance at altitude persist for at least several days after return to SL to the detriment of $\dot{V}O_2$ max. We concluded that ventilatory control is not lost under severe, progressive hypoxia; that a strong response is paramount to maintaining $\dot{V}O_2$ max; and that ventilation may be more critical than circulation in preserving $\dot{V}O_2$ max.

OPERATION EVEREST II: IMPORTANCE OF VENTILATION IN DEFENSE OF MAXIMAL OXYGEN UPTAKE AT EXTREME ALTITUDES

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ABSTRACT

The role of ventilation in the reduction of maximal aerobic power was studied in 8 subjects exposed to progressive simulated altitudes of 3962, 6096, 7468, and 8839 m (barometric pressures of 464, 347, 289, and 240 Torr, respectively), as members of Operation Everest II, a 40-day simulated ascent of Mt. Everest. The mean (±SEM) maximal oxygen uptake ($\dot{V}O_2$ max) was decreased from 4.13±0.20 at sea level (SL) to 1.2±0.08 l/min at P_B 240 Torr. Maximal heart rate also decreased from 175±6 to 127±6 bpm while arterial oxygen saturation was reduced from 97±1 to 35±3 %. Maximal exercise ventilations ($\dot{V}E$, 177±7 at SL and 185±13 l/min at P_B 240) were higher at all barometric pressures with a significant increase occurring at 464 Torr (201±9 l/min). Both frequency (f) and tidal volume (T_V) affected the increase in $\dot{V}E$ max with the f tending to be higher and T_V lower for any $\dot{V}E$ at SL. A higher correlation was found between SaO_2 and $\dot{V}O_2$ max (r=0.91) than with heart rate and $\dot{V}O_2$ max (r=0.69). The rank order of subjects for $\dot{V}E/\dot{V}O_2$ at SL was essentially the same as that at 240 Torr. $\dot{V}O_2$ max was reduced in all subjects 2 days after return to SL reaching 82 % of the original mean while associated values for $\dot{V}E$, f and T_V were not different, suggesting that responses which improve or maintain exercise performance at altitude persist for at least several days after return to SL to the detriment of $\dot{V}O_2$ max. We concluded that ventilatory control is not lost under severe, progressive hypoxia; that a strong response is paramount to maintaining $\dot{V}O_2$ max; and that ventilation may be more critical than circulation in preserving $\dot{V}O_2$ max.

Index terms: hypoxia, exercise, arterial O_2 saturation, tidal volume, breathing frequency, heart rate

INTRODUCTION

Although maximal aerobic power decreases with increasing high-altitude exposure (Refs. 16, 30, 31), maintaining maximal ventilation has always been considered an important mechanism in limiting the amount of the decrease (16, 17, 20, 30). The magnitude of the decrease in maximal oxygen uptake ($\dot{V}O_2$ max) for the highest point on earth has been estimated from theoretical analyses (3, 27) and has been predicted from measurements in two subjects breathing low oxygen mixtures at 6300 m during a climb of Mt. Everest (30). Measurements in subjects on the actual summit of Mt. Everest have not yet been possible. An approach to such measurements was made possible by Operation Everest II in which eight men participated in a simulated ascent of Mt. Everest by living in an altitude chamber over a 40-day exposure to progressive hypobaric hypoxia. The resulting study allowed measurements under relatively safe and controlled conditions not currently possible in mountain environments.

The importance of this study is to report, for the first time, repeated measurements of $\dot{V}O_2$ max and related ventilatory parameters in the same individuals progressively exposed to barometric pressures (P_B) ranging from sea level to 240 Torr, equivalent to the summit of Mt. Everest. If $\dot{V}O_2$ max were relatively well defended at high altitude, and if ventilation were important in that defense, then one might expect the following findings:

a. The $\dot{V}O_2$ max would fall less than the fall in inspired oxygen tension with decreasing P_B.

b. Maximal ventilation would be maintained with increasing altitude to near the limits of human tolerance of chronic hypoxia.

c. The capacity for exercise would be closely related to the arterial oxygen saturation, which is a key consequence of the ventilatory effort.

d. The oxygen transport across the lung to the arterial blood might be a more important determinant of exercise capacity than circulatory transport under conditions of severe, increasing chronic environmental hypoxia.

If d. above is true, then the factors limiting oxygen transport at high altitude may differ from those at sea level and may be operative in trained athletes performing maximal work. We considered that a description of human performance at extreme altitudes would provide clues to these problems which relate to oxygen uptake and utilization in hypoxia.

METHODS

The present study was of $\dot{V}O_2$ max in eight male volunteers who, over a 40-day period, made a simulated "ascent of Mt. Everest" in the decompression chamber at the United States Army Research Institute of Environmental Medicine at Natick, Massachusetts, as described in detail in other reports (6, 13, 23, 25). Each subject was informed of the nature and the risks of this study and voluntarily consented to participate. Detailed measurements relating to the circulation with cardiac catheterization (6), to alveolar (13) and blood gas (13) tensions, and to pulmonary oxygen transport (25) are reported elsewhere. Our purpose here was to measure $\dot{V}O_2$ max at various barometric pressures throughout the study and at the summit. In so far as possible, $\dot{V}O_2$ max determinations were on days separate from, but at barometric pressures approximating, those of the cardiac catheterization measurements. Thus, some comparisons could be made between resting and submaximal $\dot{V}O_2$ measured during catheterization and the values obtained during maximal exercise at relatively the same barometric pressures. Both $\dot{V}O_2$ max and

cardiac catheterizations were obtained at the barometric pressures of 760 (sea level, P_{IO2}=150 Torr), 347 (6100 m, P_{IO2}=63 Torr), and 240 Torr (P_{IO2}=43 Torr, 8840 m). $\dot{V}O_2$ max measured at a P_B of 289 Torr (7450 m, P_{IO2}=53 Torr) were compared to $\dot{V}O_2$ measured during the cardiac catheterization at 282 Torr. Measurements of $\dot{V}O_2$ max at a P_B 464 Torr had no cardiac catheterization counterpart.

Measurements of $\dot{V}O_2$ max were made using a discontinuous protocol (11). Initially, at sea level, the subject cycled at an intensity of 103 watts and the heart rate during the 5th min was used to estimate $\dot{V}O_2$ max by the method of Astrand and Rhyming (1). After a rest of at least 20 min, the subject cycled for 5 min at an workload calculated as

$$W = (\dot{V}O_2max/2) + 180$$

where W = $kg \cdot m \cdot min^{-1}$ and $\dot{V}O_2$ = $ml \cdot min^{-1}$. The procedure was repeated until an increase in intensity of 1 $kg \cdot m \cdot min^{-1}$ (30 watts) caused an increase in $\dot{V}O_2$ less than 150 $ml \cdot min^{-1}$. The $\dot{V}O_2$ max was the highest value during a 30-sec sampling period for an exercise at least 2 min in duration. We were able to satisfy these criteria for maximal oxygen uptake at all barometric pressures. For example, at the P_B of 240 Torr, we found that an increase of 30 watts in exercise intensity to either 90 or 120 watts (1.5 or 2.0 kp) failed to increase the $\dot{V}O_2$ by more than 100 $ml \cdot min^{-1}$ in all five subjects having measurements made. The above procedure was followed for all barometric pressures except that at 240 Torr $\dot{V}O_2$ max was measured in three subjects during the catheterization exercise procedure.

Because we found no previous reports of the measurement of $\dot{V}O_2$ during exercise in man breathing ambient air in an altitude chamber at these extremely low barometric pressures, details of the methods are presented. The concentrations

of oxygen and carbon dioxide in the mixed expired air were measured by a mass spectrometer (Perkin Elmer, Model 1100A and 1100B, Pomona, CA). To keep the number of molecules of gas being delivered to the mass spectrometer approximately constant as the air density fell in the altitude range from 3000 to 6000 m, a capillary tube slightly larger (0.033 in. i.d.) in diameter than usual (0.019 in. i.d.) was utilized. Above 6000 m, an even larger diameter tube (0.040 in. i.d.) was utilized. These capillary tubes exited the chamber to the mass spectrometer which was always at normobaria. On initiating measurements at 347 Torr, we noted water condensation in the capillary tube, probably reflecting the relatively high humidity (up to 80%) requested by the subjects. The mixed expired air was then dried by passing it through a column of calcium chloride (Drierite^{R}) prior to its being drawn into the mass spectrometer capillary tube. Passing the calibrating gases containing CO_2 through the Drierite^{R} was found not to alter their reading by the mass spectrometer. At the barometric pressures of 347 Torr and below, a slight alinearity was found in the calibration curve. The mass spectrometer was then calibrated using five calibration gases whose composition was verified at sea level by comparison with gases analyzed by the micro-Scholander technique. The oxygen calibration gas ranged from 21 to 1%, and from 1 to 8% for CO_2. At the extremely low barometric pressures of 282 and 240 Torr, mixed expired gas concentrations measured by the mass spectrometer were periodically confirmed by independent analysis of expired samples collected in an air tight syringe and analyzed by a calibrated IL 282 CO-oximeter analyzer (Instrumentation Laboratories, Lexington, MA).

There was also concern that the supplemental oronasal oxygen breathed by investigators using constant-flow oxygen masks at the higher altitudes (P_B less than

522 Torr) might increase the ambient oxygen concentration in the chamber. Although the chamber ambient oxygen concentration at 347 and 282 Torr was maintained at 21%; at the P_B of 240 Torr, the concentration occasionally rose to 22%. This rise occurred primarily because only the smaller chamber containing the subjects under investigation and several investigators was decompressed to 240 Torr, while the larger chamber containing the other subjects remained at the higher pressure of 282 Torr. The ventilation of the smaller chamber was sufficient to prevent the rise in ambient oxygen. The ambient concentrations of the inspired gases were measured by mass spectrometer prior to each series of $\dot{V}O_2$ measurements and were verified periodically by CO-oximeter at sea level of gas collected in the chamber. The P_B of 240 Torr was selected to give an inspired oxygen tension of 42-43 Torr, considered to be equivalent to that at the summit of Mt. Everest (28, 29).

The volume measurement of expired air utilized a Parkinson-Cowan (Model CD-4) dry gas meter. Each 10 liters of gas passing through the instrument caused one revolution of the indicator needle and reset a potentiometer to zero. Because the potentiometer output was alinear, the time required for serial 10-liters volumes was summed and used to compute the minute volume. When the computer was used to collect dry gas data, a trinomial equation was used to correct for partial potentiometer readings. Even at the extremes of altitude studied, 10 liters of air, injected as repeated 1-liter boluses, was registered as 10 liters by the meter, recorder, and/or computer.

Arterial oxygen saturations were measured by ear oximeter (Hewlett Packard Model 47201-A, Lexington, MA). Ear oximeter oxygen saturations ranging from approximately 100% to 28% could be corrected with good confidence to arterial blood oxygen saturations by the regression equation:

$$SaO_{2\ ear} = 1.10 \times SaO_{2\ blood} - 9.2$$

where N = 299 data points collected from 8 subjects at varying barometric pressures.

At the lowest P_B, the ear oximeter saturations during maximal exercise were all less than 40% and thus were on, or near, the non-identity portion of the calibration curve. An ear oximeter reading of 40% corresponded to an arterial blood value of 49%. While ear oximeter values less than 40%, Tables 1 and 2, could be corrects to blood values less than 49%, the saturations reported in this low range are still approximate.

Data were collected and analyzed by two methods. During the Swan-Ganz procedure, analog data from the dry-gas meter ($\dot{V}_E$), mass spectrometer ($\%O_2$, $\%CO_2$) and ear oximeter (SaO_2) were recorded continuously with temperature of expired air entering the P-C meter recorded as necessary for corrections to BTPS and STPD conditions. For most of the exercise measurements, all data were digitized, stored, and analyzed using an MINC 1123 computer system (Digital Equipment Corp, Maynard, MA) and displayed and printed every 30 sec. Three-lead electrocardiograms were monitored using an ECG monitor (78304A, Hewlett-Packard, Lexington, MA) and heart rate determined and displayed using a heart rate monitor (CT-4600, IBS Corp.,Waltham, MA).

While the data are presented for all individuals, analysis is centralized on the five individuals having $\dot{V}O_2$ max measurements at each of the five barometric pressures studied. Comparison by individual and by altitude could be done by two-way repeated measures analyses of variance in that there were no missing data. The correlation between two variables was determined by regression analysis. The comparison between two variables was by paired t test. A p value of 0.05 or less was considered significant. Measurements in the text and tables are presented as mean and standard error of the mean.

RESULTS

With the progressive decrements in P_B, there were associated progressive decrements in the absolute maximal workload that could be accomplished and in the $\dot{V}O_2$ max. At the time of reduced $\dot{V}O_2$ max, the subjects also had reductions in carbon dioxide output, heart rate, and arterial oxygen saturation (Table I). All eight subjects were studied at sea level and at a P_B of 464 Torr, but at the barometric pressures of 347 and lower, subjects 5 and 7 had been removed from the chamber. Subjects 5 and 7 had the highest $\dot{V}O_2$ max ($ml \cdot kg^{-1} \cdot min^{-1}$) at sea level (Table I). Subject 9, with the lowest $\dot{V}O_2$ max ($ml \cdot kg^{-1} \cdot min^{-1}$), completed the 40-day altitude exposure and exercised at an intensity of 30 W at the P_B of 240 Torr, but elected not to perform the $\dot{V}O_2$ max test. At sea level, the $\dot{V}O_2$ max ranged from 41.3 to 63.3 ($ml \cdot kg^{-1} \cdot min^{-1}$), a span of 22. For the two lowest barometric pressures, 289 and 240 Torr, the range spanned only 7 ($ml \cdot kg^{-1} \cdot min^{-1}$), Table I.

The range of $\dot{V}O_2$ max between individuals also decreased with P_B in the five subjects who had measurements at each of the five pressures studied, including pressure equivalent to the summit of Mt. Everest. For these five subjects, the group means, Tables 2 and 3, do not contain missing data, and the subjects served as their own controls. From sea level to the lowest P_B studied, the fall in $\dot{V}O_2$ max (4128 to 1172 $ml \cdot min^{-1}$) of 72% was comparable to the fall in workload (6.1 to 1.7 kp) of 72%, and the fall in inspired oxygen tension (149 to 43 Torr) of 71%, Table II. Maximal heart rate during maximal exertion also fell with decreasing pressure but from 175 to 127 bpm (29%). Arterial oxygen saturation, as measured by ear oximeter, fell from 97% to 35%, a difference of 62%.

During $\dot{V}O_2$ max as P_B was lowered, minute ventilation ($\dot{V}_E$) did not decrease (Table II). In fact, at the P_B of 464 Torr, ventilation was slightly but significantly increased above the sea-level value. When ventilations at rest and during submaximal exercise, from Table III, were examined in relation to those at maximum effort, curves were obtained which indicated that ventilations for the whole range of $\dot{V}O_2$ were shifted to higher values at the reduced barometric pressures, Fig. 1A.

At sea level, increases in both respiratory frequency and tidal volume (V_T) contributed to the increased ventilation as the subjects exercised at submaximal workloads and maximal effort (Table II and III). For each submaximal workload at the reduced barometric pressures, both frequency and V_T were higher than at sea level (Table III). However, the analysis by workload did not establish the relative contributions of frequency and V_T to the increased ventilation during exercise at reduced pressures. For a given ventilation, frequencies tended to be higher and V_T tended to be lower, than at sea level, Fig. 2A. The relationship of V_T to frequency appeared to be shifted to higher frequencies at the reduced barometric pressures, Fig. 2A, suggesting that the increased ventilation during exercise at high altitude received a somewhat greater contribution from frequency than from V_T.

If a marked increase in ventilation at high altitude acts to maintain arterial oxygenation, which in turn, is key for exercise capacity at high altitude (16,17,30), then a marker of arterial oxygenation should be closely related to $\dot{V}O_2$ max. Indeed, we found that arterial oxygen saturation showed a strong relation to $\dot{V}O_2$ max, Fig. 3A. At the highest altitude (P_B=240 Torr), the range in saturations by ear oximeter was from 27 to 42%, Table I. Even though, in this low range, the ear oximeter may have underestimated the blood saturation there was little

interindividual variation. The simultaneously measured heart rate also correlated with $\dot{V}O_2$ max (Fig. 3B). However, a large range of maximal heart rates was observed at each of the barometric pressures. In particular at 240 Torr, the rates ranged from 112 to 148 bpm (Table I). Thus, the correlation coefficient was higher for the relation of $\dot{V}O_2$ max to arterial saturation than to heart rate (Fig. 3).

Given the potential importance of ventilation for maximal exercise performance at high altitude, could the observed level of ventilation at extreme altitude be predicted from low altitude measurements? One measure of relative level of ventilation is the oxygen ventilatory equivalent, $\dot{V}_E/\dot{V}O_2$, (Table I). During $\dot{V}O_2$ max, the oxygen ventilatory equivalent at sea level ranged from 35 to 53. At the lowest P_B during maximal exercise, the rank order of subjects for oxygen ventilatory equivalents was almost the same as that observed at sea level, and the values for these two extremes of altitude were closely related, Fig. 4. Relationships were also present but not as apparent for the intermediate barometric pressures of 464, 347, and 289 Torr.

Six subjects who completed the 40-day altitude exposure had measurements of $\dot{V}O_2$ max within 2 days of return to sea level. The workload which could be accomplished was reduced or unchanged in five of them and was slightly increased in the sixth. $\dot{V}O_2$ max and body weights, however, were reduced in all six, as was the $\dot{V}O_2$, normalized by body weight (Table IV). Heart rate was reduced, but ventilation, frequency, V_T, and respiratory quotient were not changed.

DISCUSSION

The main result of the present study was that under conditions of extreme hypobaric hypoxia simulating the summit of Mt. Everest, 240 Torr, a sustained high

level of ventilation (due more to frequency than V_T) during maximal exercise contributed to the relatively well maintained $\dot{V}O_2$ of 15.3 $ml \cdot kg^{-1} \cdot min^{-1}$. Our measurements represent true maximal values in that our criteria for VO_2 max, an exercise intensity above which further increase did not cause the appropriate increase in $\dot{V}O_2$, was met in all cases. Also, the maximal values were identical to those predicted for the summit in two subjects at 6300 m (350 Torr) on Mt. Everest breathing low oxygen mixtures to simulate the inspired oxygen tension on the summit (30).

We noted that the tolerance of high altitude and the capacity to exercise did not depend on a high $\dot{V}O_2$ max at sea level. First, the two subjects at sea level having the highest $\dot{V}O_2$ max did not tolerate the altitude and were removed from the chamber, indicating that their sea-level performance did not ensure tolerance of high altitude. It is also noteworthy that these same two subjects had significant desaturation during their maximal exercise test at sea level (87 and 85% SaO_2 by ear oximetry). Dempsey (3) has proposed that severe exercise in well-trained athletes may cause desaturation due to maximum flow pulmonary blood flow/volume limitations resulting in reduced pulmonary capillary transit time and pulmonary diffusing capacity. It is interesting to speculate whether the mechanisms that may be operative during desaturation at sea level may also lead to reduced exercise tolerance at altitude. Next, considering only the five subjects studied at all altitudes, the variation in $\dot{V}O_2$ max between individuals was much larger at sea level than at the various high altitudes, as has been observed previously in subjects taken from sea level to 4300 m altitude (31). Also the sea-level $\dot{V}O_2$ max in the subjects of the AMREE expedition (61.3 $ml \cdot kg^{-1} \cdot min^{-1}$) (30) exceeded that of our subjects (49.1 $ml \cdot kg^{-1} \cdot min^{-1}$), suggesting that the AMREE subjects as a group were better conditioned. But when the inspired oxygen tension had fallen to 43

Torr, the maximal oxygen uptakes were the same in our subjects and those of the AMREE expedition, even though the latter had experienced the rigors and exertions of the actual mountain exposure. The fact that the $\dot{V}O_2$ max in our subjects, after return from the hypobaric exposure, was less than before the exposure, suggests that a determinant of the sea-level $\dot{V}O_2$ max had been adversely affected by the altitude exposure and that this change is not immediately reversed by normoxia. Finally, $\dot{V}O_2$ max at sea level, where there is little or no hypoxemia, may be more dependent on circulatory than pulmonary oxygen transport (3). If so, the variability in the $\dot{V}O_2$ max in sea-level subjects may be related to factors such as exercise conditioning. With the extreme ambient hypoxia at the high simulated altitudes of the present study, the ventilatory transport of oxygen from the atmosphere to the alveoli, i.e., the first link in the oxygen transport chain, could be the important determinant of the $\dot{V}O_2$ max at high altitude, as recently suggested by Schoene (20, 21), West (26), and Pugh (16, 17). From the above, we considered that the principal determinants of $\dot{V}O_2$ max at sea level were not identical to those at high altitude where ventilation may be relatively more important.

The present report, therefore, has focused on ventilation during $\dot{V}O_2$ max. Our findings that the ventilation during maximal oxygen uptake at high altitude was maintained at least as high as at sea level confirmed and extended previous reports from lesser altitudes (16) and data from the simulated summit conditions (30). We also confirmed that the maximum ventilation observed was at an intermediate altitude, in our case equivalent to a P_B of 464 Torr, rather than at more severe hypobaric hypoxia where P_B = 351 Torr and PIO_2 = 64 Torr (30). The relatively minor differences between our data and those of West et al. (30) (Fig. 5) are a more stable maximum ventilation without a marked reduction in $\dot{V}E$ max at the lowest inspired PO_2 tested and a more stable ventilatory frequency as

altitude increased. Probably the differences in the experimental conditions and the relatively few measurements previously available account for the different results.

Our analysis of ventilation considered the respiratory system as a pump with components of frequency and stroke volume delivering ambient air (oxygen) to the lung, in analogy with the cardiac pump which delivers oxygen to the tissues. We noted, as reported by Pugh (17), that ventilation for a given $\dot{V}O_2$, at rest, and during submaximal or maximal exercise was shifted to higher values with increasing altitude, compatible with increasing hypoxic stimulation of ventilation. On examining the components of ventilation, i.e., respiratory frequency and V_T for a given ventilation, mean frequency always tended to be increased at high altitude compared to sea level, while V_T tended to be decreased. Studies of the altitude effects on the components of the ventilatory response have indicated that the initial response to chronic, stable hypoxia is characterized by a greater increase in frequency rather than tidal volume followed after several days by a greater reliance on tidal volume changes (5, 7, 8, 22). However, when the hypoxic stimulus is progressive, then frequency appears to retain its relative contribution to the increased ventilation (18). Although we do not have data obtained during acute hypoxia, our measurements which approach the limits of human tolerance are consistent with the concept that respiratory frequency makes the greater contribution to ventilation when ventilatory acclimatization is altered by the progressive hypoxia of this study.

The contrasts and similarities of circulatory with ventilatory transport of oxygen are of interest. In contrast to ventilation, the cardiac output for a given $\dot{V}O_2$ at high altitude was not different from that at sea level (18), Fig. 1B, suggesting that under the conditions of these experiments, hypoxemia did not

provide as great a stimulation of cardiac output as ventilation. However, in similarity to the ventilatory pump, a given cardiac output at high altitude, compared to that at sea level (Fig. 2B), was preferentially maintained by increased frequency, i.e., heart rate, rather than by stroke volume. The respiratory and cardiac pumps are primarily responsible for the mass transport of oxygen, and apparently both preferentially utilize frequency over volume to maintain transport at high altitude.

An important question is the extent to which adaptations in the ventilatory mass transport of oxygen at high altitude succeed in preserving $\dot{V}O_2$ max. Although the literature is replete with studies on the reduction in $\dot{V}O_2$ max at high altitude (e.g., Refs. 2, 9, 12, 24, 31), one could consider that given the fall in inspired oxygen tension the capacity for oxygen transport is remarkably well preserved. For example, at the barometric pressures of 464, 347, and 289 Torr, the percent reduction in $\dot{V}O_2$ were less than the percent decreases in inspired oxygen tension (Fig. 6), implying that effective mechanisms operated to defend $\dot{V}O_2$ at these altitudes. Even at the lowest P_B, 240 Torr (P_{IO2}=43 Torr), the relative decrement in $\dot{V}O_2$ was not less than that in inspired oxygen tension. Apart from the shape of the oxyhemoglobin dissociation curve, one mechanism preserving $\dot{V}O_2$ (per unit of body weight) was the weight loss at high altitude, which decreased the denominator of the ratio under consideration. Most striking, however, was that ventilation at high altitude remained at or above the sea-level value. Apparently, despite the reduced maximal cardiac outputs at rest or with different exercise levels at the various altitudes (19, 17), the $\dot{V}O_2$ max was better maintained than was the inspired oxygen tension. The high ventilatory rate would tend to decrease the carbon dioxide tension and thereby increase alveolar oxygen tension, allowing an increased arterial oxygen saturation. The findings that even at the highest altitudes and with increasing exercise to maximum effort, alveolar oxygen tension did not fall

nor did carbon dioxide tension rise (23) implied that ventilatory effort did not fail under these extreme conditions. The close relationship of arterial saturation to $\dot{V}O_2$ max and, at the highest altitude, and the small variation between individuals in oxygen saturation is compatible with an important role for ventilation in oxygen transport. The variability at the highest altitude in both heart rate at maximum effort and in cardiac output at near maximum effort contrasted with oxygen saturation data and indicated that a given amount of oxygen could be utilized over a wide range of circulatory values. These considerations suggest that, at extreme altitudes, ventilation may be more critical than circulation in preserving the maximal oxygen uptake.

The finding that ventilation during maximal exercise at sea level related to ventilation during maximal effort at the P_B of 240 Torr is compatible with previous studies (20, 10, 14, 15). This supports the thesis that exercise ventilation is a characteristic of an individual which continues to be expressed under the conditions of the most severe hypoxemia. Thus, in view of the preserved individual ventilatory response and the progressive increase in ventilation with increasing hypoxemia at rest and during, we conclude that under these conditions of chronic, severe, progressive hypoxia ventilatory control is not lost in normally acclimatizing man. Indeed, a strong ventilatory response to hypoxemia and to exercise may be of the utmost importance in maintaining a $\dot{V}O_2$ max at great altitudes including the summit of Mt. Everest.

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TABLE I. Measurements relating to ventilation and heart rate during maximal oxygen uptake

SUBJECT	WT	WORK-LOAD	$\dot{V}_E$ Max BTPS	f	V_T BTPS	$\dot{V}O_2$ Max	$\dot{V}CO_{2Max}$	R	$\dot{V}O_2$/kg	$\dot{V}_E/\dot{V}O_2$	HR	SaO2
	kg	kp	l/min	brths/min	l	ml/min	ml/min		ml/min		b/min	%
Barometric pressure = 760 Torr PIO2 = 150 Torr												
1	100.9	6.5	163.2	45	3.63	4220	5540	1.31	41.8	38.7	183	95
3	76.7	4.5	178.0	60	2.97	3370	4740	1.45	43.9	52.8	192	100
4	84.4	7.0	194.8	60	3.25	4370	5450	1.25	51.8	44.6	161	94
5	59.4	5.5	171.9	48	2.58	3550	4030	1.14	59.7	48.4	174	87
6	84.5	6.5	190.8	60	3.18	4200	5330	1.27	49.7	45.4	165	95
7	72.7	6.5	217.4	57	3.81	4600	5660	1.23	63.3	47.3	182	85
8	77.2	6.0	157.0	63	2.49	4480	5680	1.27	58.1	35.0	175	93
9	74.1	4.5	162.2	51	3.18	3060	3230	1.06	41.3	53.0	189	94
Mean	78.7	5.9	179.4	56	3.14	3980	4960	1.25	51.2	45.7	178	93
SEM	4.2	0.4	7.2	2	0.16	200	320	0.04	3.0	2.2	4	2
Barometric pressure = 464 Torr PIO2 = 88 Torr												
1	99.0	5.8	212.9	48	4.44	2990	3580	1.20	30.2	71.2	166	57
3	76.0	3.5	199.8	84	2.38	2440	2630	1.08	32.1	81.9	190	75
4	81.0	6.0	206.6	60	3.44	2840	2690	0.95	35.0	72.7	149	74
5	58.4	4.5	207.6	66	3.15	2610	3240	1.24	44.7	79.5	166	63
6	82.0	5.5	232.5	66	3.52	3450	3770	1.09	42.0	67.4	163	63
7	72.0	5.8	224.0	60	3.73	3070	3630	1.18	42.6	73.0	174	59
8	74.2	5.0	182.9	66	2.77	2880	3290	1.14	38.8	63.5	155	64
9	73.3	4.0	222.6	90	2.47	2260	2860	1.27	30.8	98.5	182	68
Mean	77.0	5.0	211.1	68	3.24	2820	3200	1.14	37.0	76.0	168	65
SEM	4.1	0.3	5.5	5	0.24	130	160	0.04	2.0	3.8	5	2
Barometric pressure = 347 Torr PIO2 = 63 Torr												
1	94.8	3.0	160.7	57	2.82	2190	2370	1.08	23.1	73.3	136	45
3	73.6	3.0	202.9	78	2.60	2050	2470	1.21	27.8	99.0	157	61
4	76.4	3.5	206.6	60	3.44	2230	2490	1.12	29.2	92.6	135	55
5	58.4	3.0	177.6	63	2.82	1770	2400	1.35	30.3	100.3	148	24
6	79.3	3.5	230.7	72	3.20	2450	2950	1.21	30.9	94.2	145	44
8	74.0	3.0	183.1	63	2.91	2120	2820	1.33	28.7	86.4	131	53
9	72.4	2.5	147.6	60	2.46	1600	2040	1.28	22.1	92.3	148	46
Mean	75.6	3.1	187.0	65	2.89	2060	2510	1.23	27.4	91.2	143	47
SEM	4.1	0.1	10.8	3	0.13	110	110	0.04	1.3	3.4	3	3
Barometric pressure = 289 Torr PIO2 = 53 Torr												
1	94.1	3.0	175.0	63	2.78	1990	2290	1.04	19.8	87.9	152	32
3	72.7	2.5	200.8	87	2.31	1760	1880	1.02	22.1	114.1	161	42
4	76.4	2.5	197.1	60	3.29	1830	1520	0.83	21.5	107.0	120	53
5	57.3	2.5	191.8	69	2.78	1540	1790	1.15	26.9	124.5	148	26
6	77.0	3.0	222.2	72	3.09	1880	1850	0.98	21.9	118.2	124	51
8	72.5	2.5	163.7	60	2.73	1810	1900	1.04	21.9	90.4	121	33
9	70.9	2.0	180.9	66	2.74	1610	1640	1.02	21.6	112.4	164	35
Mean	74.4	2.6	190.2	68	2.82	1770	1830	1.03	22.3	107.9	141	39
SEM	4.1	0.1	7.2	4	0.12	60	90	0.04	0.8	5.2	7	4

Barometric pressure = 240 Torr PIO2 = 43 Torr

1	91.0	2.0	147.2	51	2.89	1020	1350	1.33	11.2	144.3	133	27
3	70.6	1.5	194.8	60	1.58	960	1140	1.20	13.6	202.9	148	32
4	76.4	2.0	201.3	60	3.36	1240	1330	1.08	16.2	162.3	120	39
6	75.9	2.0	219.2	78	2.81	1390	1480	1.06	18.2	158.8	112	36
8	72.0	1.0	164.1	66	2.49	1250	1130	0.91	17.4	131.3	124	42
Mean	77.3	1.7	185.3	63	2.62	1170	1286	1.12	15.3	159.9	127	35
SEM	3.6	0.2	13.0	4	0.30	80	67	0.07	1.3	12.1	6	3

Table II. Summarized cardiorespiratory data during maximal oxygen uptake for five subjects studied at all barometric pressures

	P_B	Wt	Work-Load	$\dot{V}_{E\,Max}$ BTPS	f	V_T BTPS	$\dot{V}O_{2\,Max}$	$\dot{V}CO_{2Max}$	R	$\dot{V}O_2$/kg	HR beats/	SaO2
	Torr	kg	kp	l/min		l	ml/min	ml/min		ml/min	min	%
Mean	760	84.5	6.1	177	58	3.1	4128	5348	1.31	49.1	175	97
SEM		4.5	0.4	7	3	0.2	196	162	0.04	2.9	6	1
Mean	464	82.5	5.2	201	66	3.3	2916	3176	1.09	35.6	165	72
SEM		*4.4	*0.4	*9	5	0.4	*162	*240	*0.04	*2.2	*7	*5
Mean	347	79.6	3.2	192	64	3.1	2208	2620	1.19	27.9	136	59
SEM		*3.9	*0.1	14	4	0.2	*68	*112	0.04	*1.3	*4	*1
Mean	289	78.6	2.7	187	68	2.7	1688	1966	1.17	21.6	133	48
SEM		*3.9	*0.1	11	6	0.2	*45	*11	0.03	*0.5	*8	*3
Mean	240	77.3	1.7	185	63	2.6	1172	1286	1.12	15.3	127	35
SEM		*3.6	*0.2	13	4	0.3	*79	*67	*0.07	*1.3	*6	*3

*Indicates measurement at reduced barometric pressure is different ($P<0.05$) from sea-level value

TABLE III. Measurements relating to ventilation during submaximal exercise: mean values (SEM) for five subjects

P_B Torr	WORK-LOAD kp	$\dot{V}_E$ BTPS l/min	f breaths/ min	V_T BTPS l	$\dot{V}O_2$ ml/min	$\dot{V}CO_2$ ml/min	R
760	0	10.7	10.9	1.00	355	258	0.73
	0	0.5	0.8	0.06	29	19	0.03
	1	31.1	20.5	1.61	1252	966	0.77
	0	2.1	3.1	0.16	67	45	0.02
	2	48.0	27.8	1.77	1827	1560	0.85
	0	1.6	2.8	0.11	64	74	0.03
	2.9	64.7	31.3	2.11	2450	2188	0.90
	0.1	3.3	2.9	0.14	84	33	0.03
	3.9	88.4	35.6	2.61	3162	2976	0.95
	0.1	6.6	5.9	0.21	95	68	0.05
347	0	20.0	18.9	1.09	308	271	0.89
	0	3.1	2.4	0.13	36	27	0.02
	1	50.0	34.0	1.61	943	818	0.89
	0	1.7	5.9	0.20	46	40	0.05
	2	91.6	40.1	2.37	1525	1459	0.97
	0	6.1	4.8	0.22	89	69	0.05
282	0	36.6	28.4	1.29	406	352	0.87
	0	3.5	2.8	0.05	16	16	0.04
	1	94.3	49.7	2.08	957	954	1.00
	0	7.5	6.7	0.22	33	30	0.03
	1.8	151.0	56.7	2.68	1445	1511	1.05
	0.1	9.8	3.9	0.11	66	44	0.04
240	0	45.1	27.6	1.68	386	369	0.96
	0	1.6	2.2	0.16	17	25	0.03
	1	131.6	57.7	2.30	927	1042	1.13
	0	11.3	5.8	0.07	39	18	0.06

TABLE IV. Measurements on return to sea level: change from initial sea-level values

SUBJECT	WT	WORK-LOAD	$\dot{V}_E$ BTPS	f	V_T BTPS	$\dot{V}O_{2\ Max}$	$\dot{V}CO_{2Max}$	R	$\dot{V}O_2$/kg	HR
	kg	kp	l/min	breaths/min	l	ml/min	ml/min		ml/min	beats/min
1	-6.8	-0.5	-13.2	0	-0.05	-850	-1480	-0.10	-6.1	-9
3	-5.0	0.3	-1.9	6	-0.31	-590	-1230	-0.18	-5.1	-9
4	-8.0	-0.5	-19.8	0	-0.33	-1360	-1690	0.00	-12.4	-14
6	-7.2	0.0	3.9	3	-0.07	-430	-890	-0.09	-0.9	3
8	-5.6	-0.5	-26.0	-12	-0.14	-910	-2420	-0.36	-9.3	-17
9	-2.4	-0.3	15.7	8	0.32	-90	120	0.07	-0.2	-1
Mean	-5.8	-0.3	-6.9	1	-0.10	-710	-1270	-0.11	-5.7	-8
SEM	.8	0.1	6.4	3	0.10	180	350	0.06	1.9	3

LEGENDS

Figure 1. Measurements relating to minute ventilation, $\dot{V}E$, (A,upper panel) and to cardiac output (B, lower panel) at high altitude.

A. $\dot{V}E$ BTPS as related to oxygen uptake ($\dot{V}O_2$). Shown for five subjects having measurements at all barometric pressures, are mean values at rest and during submaximal exercise from Table III, and mean values during $\dot{V}O_2$ max from Table II. For a given $\dot{V}O_2$, there is a progressive increase in $\dot{V}E$ as barometric pressures are reduced.

B. Shown for comparison to the ventilatory measurements is the relation of cardiac output to $\dot{V}O_2$ for the five subjects in Fig. 1A, where the mean values were computed from data for the same subjects as reported elsewhere (6). All five subjects are represented at sea level; subjects 1,3,6,and 8 are represented at P_B 347 Torr (except subject 3 did not perform the highest exercise level); and subjects 1,3,4, and 8 at P_B 282 and 240 Torr. Submaximal exercise cardiac outputs are independent of barometric pressures.

Figure 2. Measurements of the components of ventilation for the five subjects of Fig. 1, at various barometric pressures, i.e., respiratory frequency and $\dot{V}T$, panel A, left, and analogous measurements, panel B, right, relating to circulation (cardiac output), i.e., heart rate, and stroke volume.

A, left, Ventilation. Shown, top, is the relation of frequency to $\dot{V}_E$. Middle, is the relation of $\dot{V}T$ to ventilation. Shown, bottom, is the relation of $\dot{V}T$ to frequency.

B, right, Circulation. Shown, top, are measurements for comparison with ventilation of the relation of heart rate to cardiac output. Shown, middle, is the relation of stroke volume to cardiac output. Symbols, the data source, and the number of measurements are as in Fig. 1B.
With regard to both ventilation and circulation, note the greater reliance on frequency parameters compared to unit volumes under hypoxic conditions

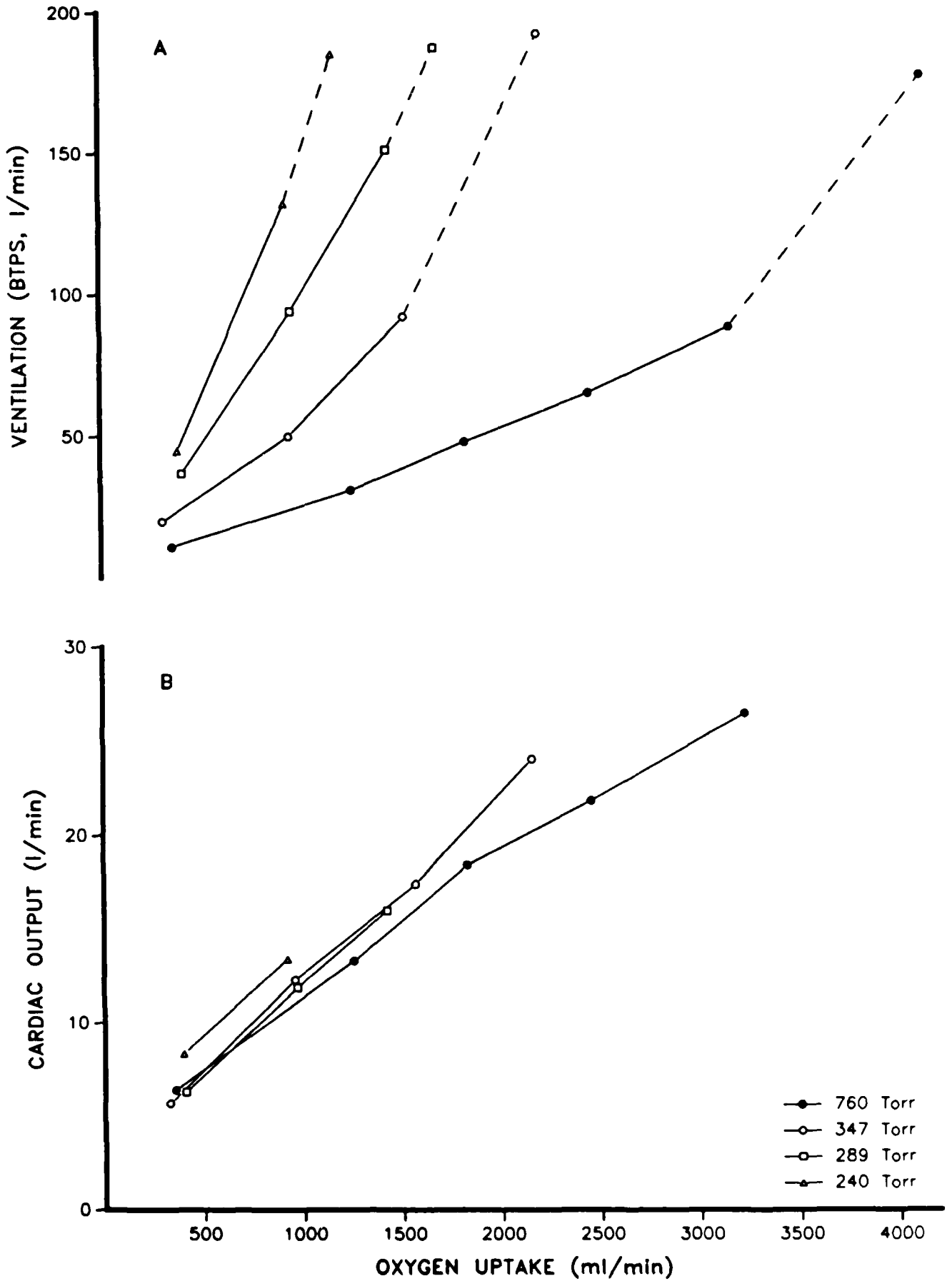
Figure 3. A, Left. The relation of $\dot{V}O_2$ max per kilogram of body weight to arterial oxygen saturation measured at the time of the maximal oxygen uptake. Shown are individual data for the five subjects with each subject having a measurement at each of the five barometric pressures (760, 464, 347, 289, and 240 Torr). The least squares line of best fit, and the correlation coefficient, r, for the 25 measurements are shown.
B, Right. Relation of $\dot{V}O_2$ max to heart rate measured at the time of the $\dot{V}O_2$ max. Measurements for Fig. 3A and 3B are from Table I. Note the higher correlation of $\dot{V}O_2$ max with arterial O_2 saturation than with heart rate.

Figure 4. The relationship of the oxygen ventilatory equivalent ($\dot{V}_E/\dot{V}O_2$ max) at the P_B of 240 Torr to that measured at sea level. Shown are the measurements for the five individuals (subject number indicated in parentheses) having measurements made at both barometric pressures. The least squares line of best fit, the correlation coefficient, r, and the

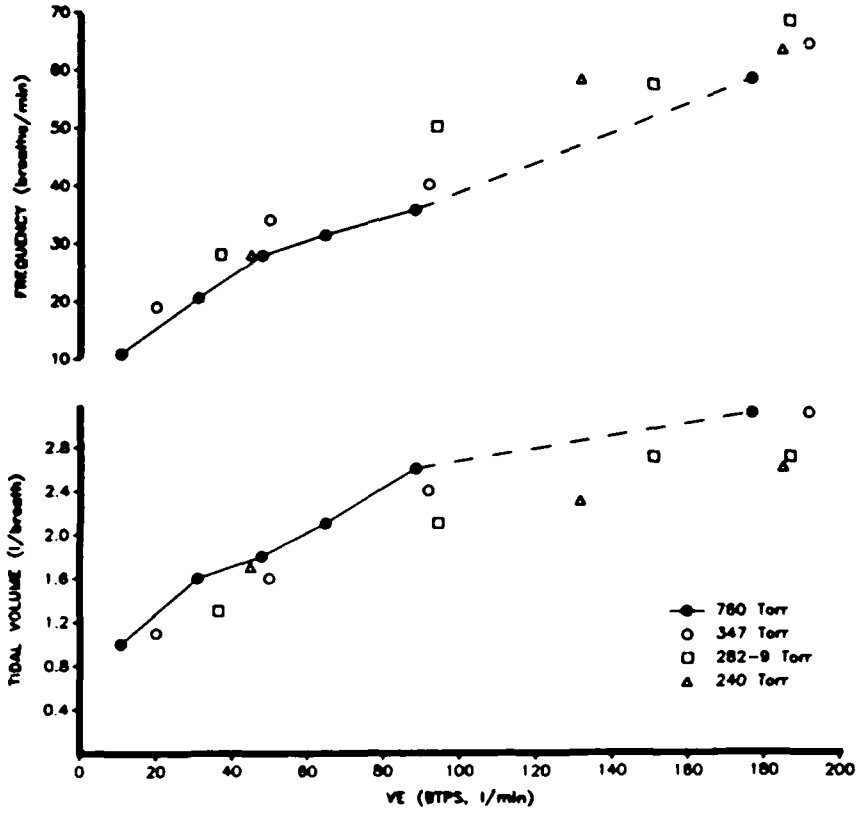
p value are indicated. Note that the rank order of the ventilatory equivalent at P_B 240 Torr was almost the same as that obtained at sea level.

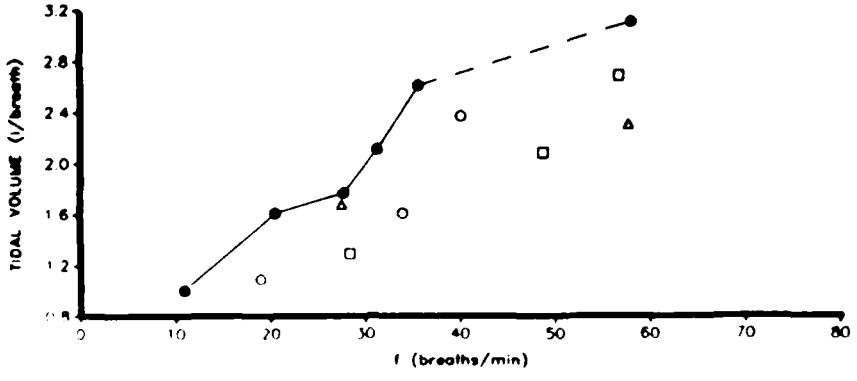
Figure 5. Relationships of $\dot{V}_E$ and respiratory frequency (f) as measured during $\dot{V}O_2$ max to inspired oxygen tension at sea level (P^IO_2 = 150 Torr) and high altitude (P_IO_2 < 150 Torr). Shown are ventilation (triangles) and respiratory frequency (circles) as related to inspired oxygen tension on a logarithmic scale. The figure was constructed from the data of the present report, Table II, for the five subjects having $\dot{V}O_2$ max at all five barometric pressures. The data of West et al.(30) from the 1981 AMREE expedition (dashed lines) are plotted for comparison.

Figure 6. Relationships of $\dot{V}O_2$ max per kilogram body weight and $\dot{V}_E$ to inspired oxygen tension at sea level and high altitude. Both abscissa and ordinate are expressed as percent of sea-level values. Variables which decreased exactly with the decrease in inspired oxygen tension would fall along the line of identity, shown. Ventilation showed no appreciable decrease, and the decrease in $\dot{V}O_2$ max was less than the decrease in inspired oxygen tension.

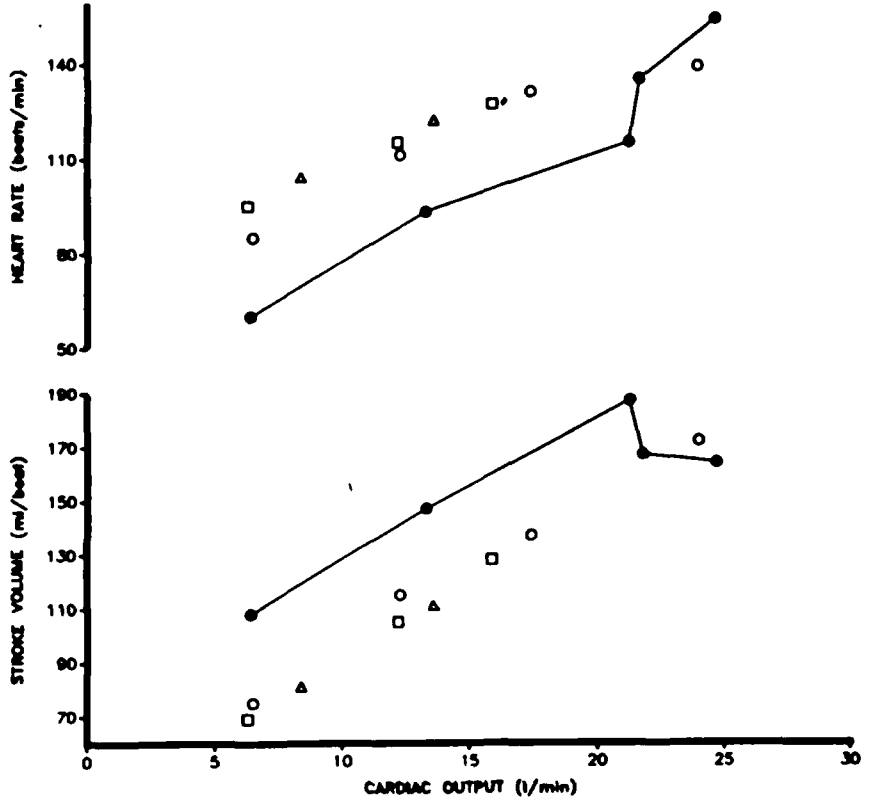

A
B
VENTILATION (BTPS, l/min)
CARDIAC OUTPUT (l/min)
OXYGEN UPTAKE (ml/min)
200
150
100
50
30
20
10
0
500
1000
1500
2000
2500
3000
3500
4000
760 Torr
347 Torr
289 Torr
240 Torr

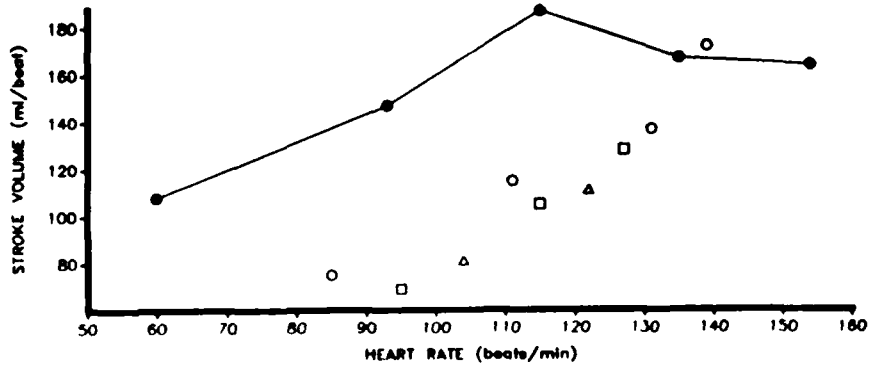
A. VENTILATION

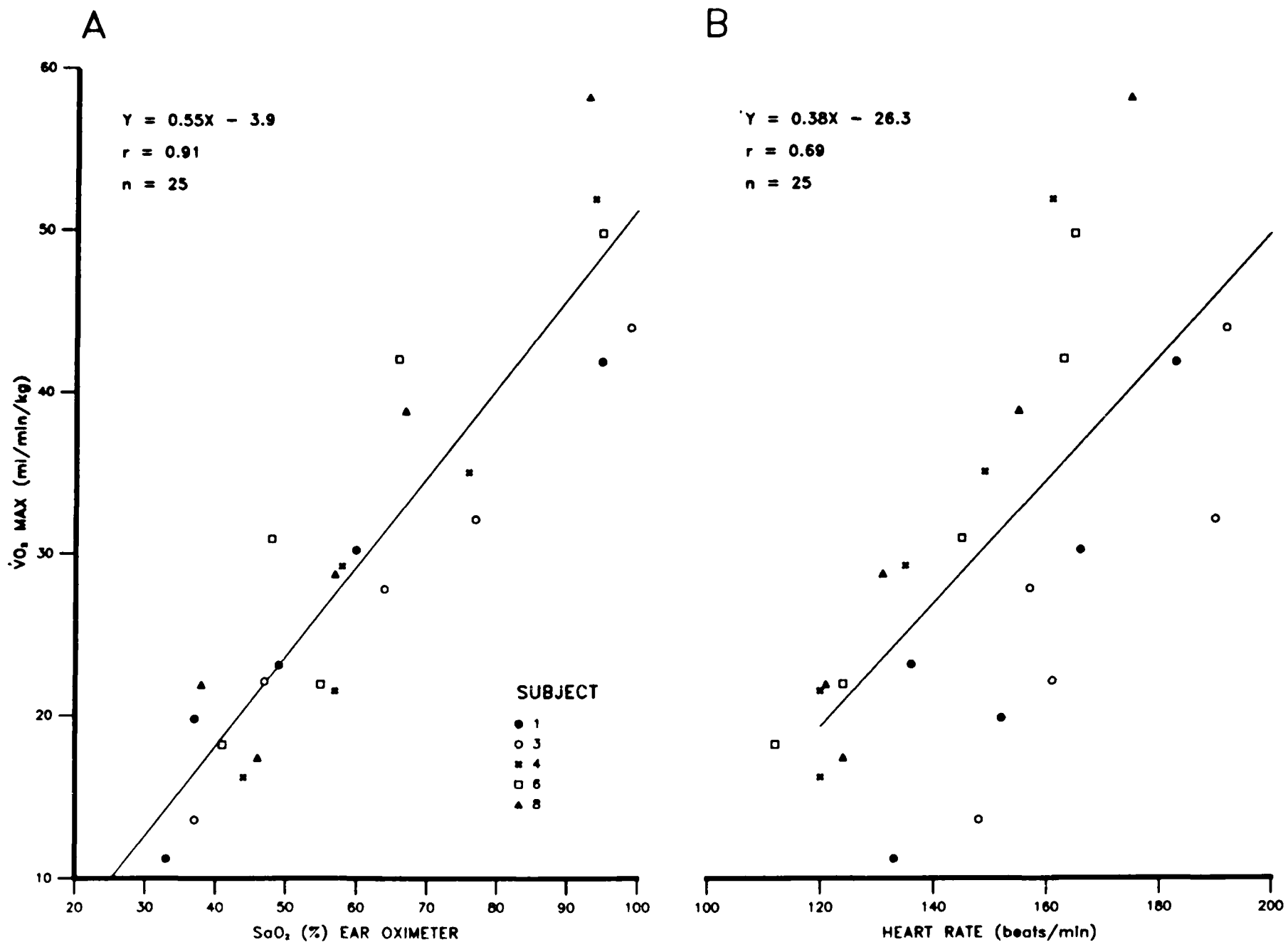


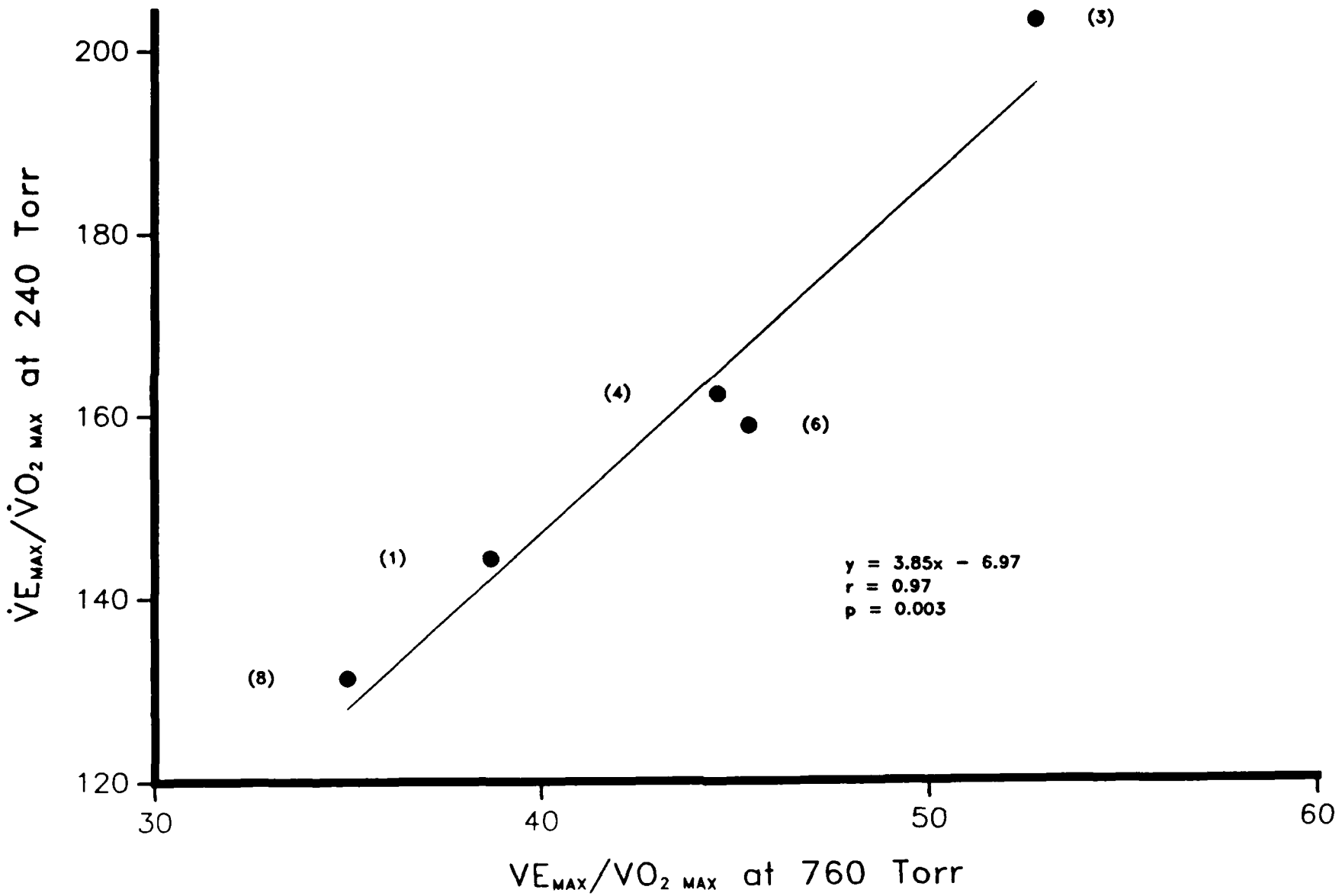


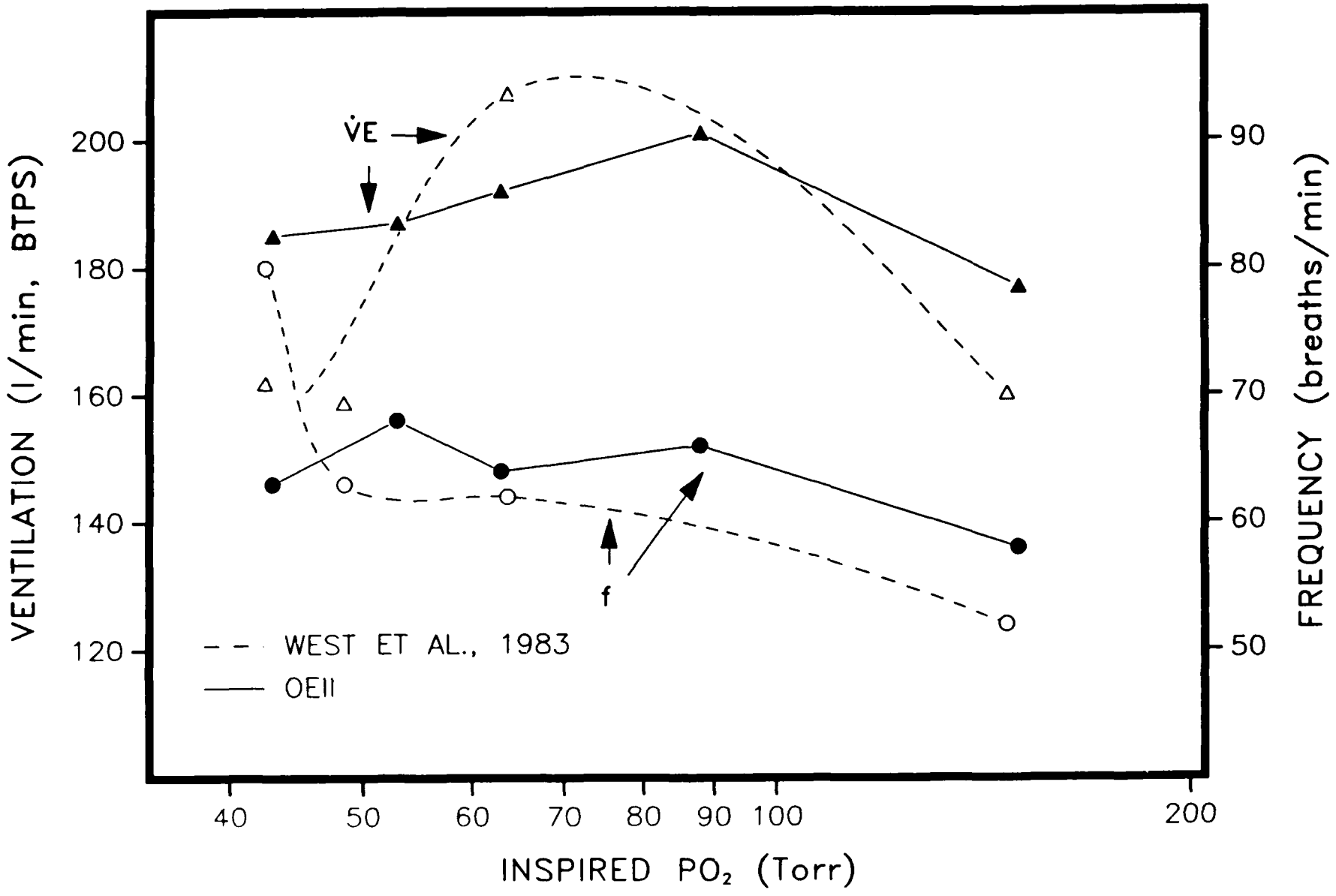
B. CIRCULATION

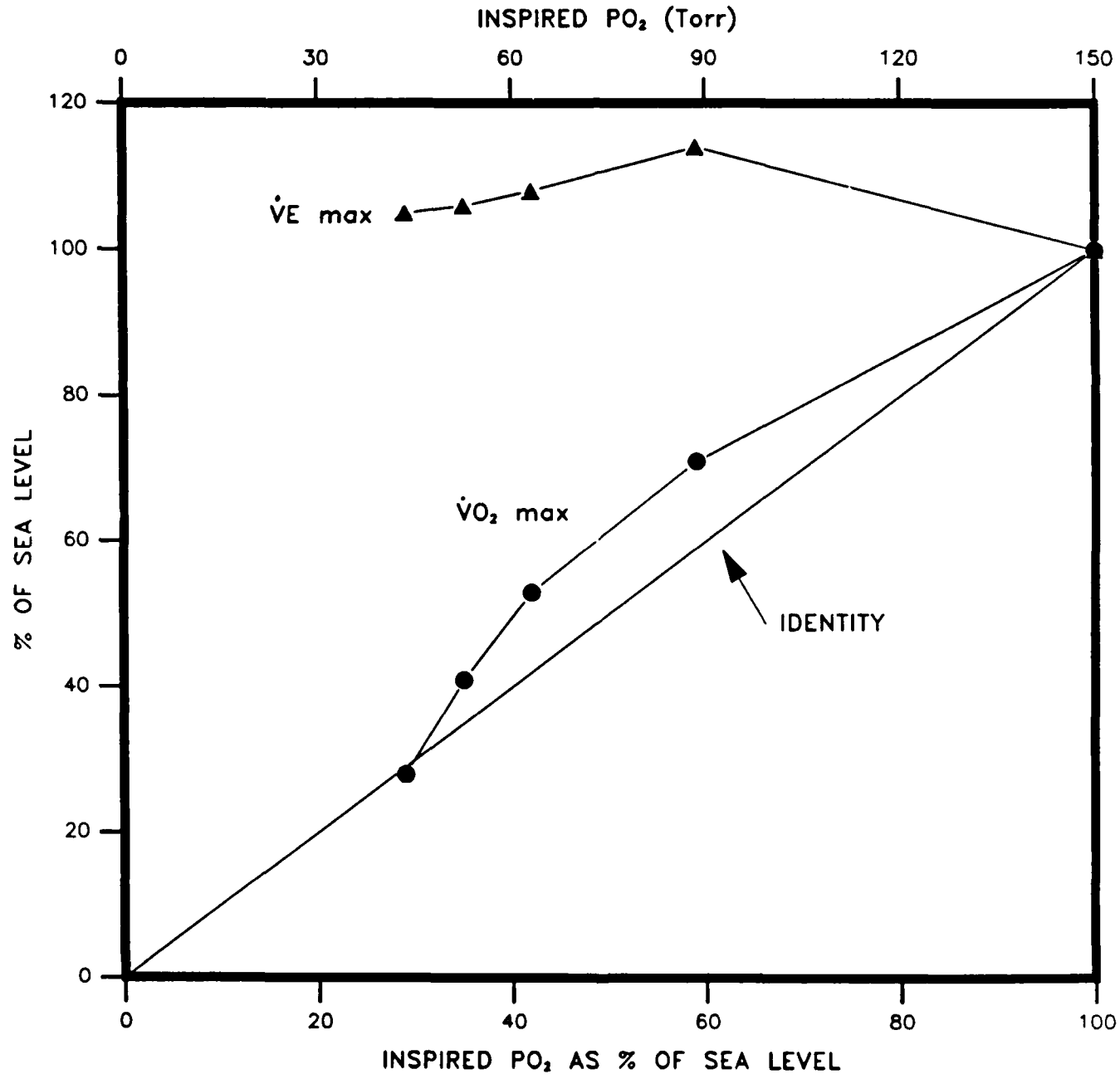





A
Y = 0.55X - 3.9
r = 0.91
n = 25
$\dot{V}O_2$ MAX (ml/min/kg)
60
50
40
30
20
10
20
30
40
50
60
70
80
90
100
SaO_2 (%) EAR OXIMETER
SUBJECT
1
3
4
6
8
B
Y = 0.38X - 26.3
r = 0.69
n = 25
100
120
140
160
180
200
HEART RATE (beats/min)


200
180
160
140
120
30
40
50
60
$\dot{V}E_{MAX}/\dot{V}O_{2\ MAX}$ at 240 Torr
$VE_{MAX}/VO_{2\ MAX}$ at 760 Torr
(1)
(3)
(4)
(6)
(8)
y = 3.85x - 6.97
r = 0.97
p = 0.003


VENTILATION (l/min, BTPS)
FREQUENCY (breaths/min)
INSPIRED PO_2 (Torr)
$\dot{V}E$
f
WEST ET AL., 1983
OEII
200
180
160
140
120
90
80
70
60
50
40
50
60
70
80
90
100
200


INSPIRED PO_2 (Torr)
0
30
60
90
120
150
120
100
80
60
40
20
0
% OF SEA LEVEL
$\dot{V}E$ max
$\dot{V}O_2$ max
IDENTITY
0
20
40
60
80
100
INSPIRED PO_2 AS % OF SEA LEVEL

END

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DTIC